

nucleotide sequence immediately upstream of the ATG codon including. . . J. Rossi et al., 1982; J. Biol. Chem. 257, 9226-9229) and converted into a double-stranded DNA molecule by incubation with **Klenow** DNA polymerase and the four dNTP's under conditions which have been described for double-stranded DNA synthesis (A. R. Davis et. . . products by electrophoresis through a 13% acrylamide gel followed by autoradiography showed that more than 80% of the starting single-stranded **oligonucleotides** were converted into double-stranded material. The DNA was isolated by passage of the reaction mix over a Sephadex G50 column. . .

=> d 1-2 cls
=> d 1-2 cls

4,885,166 424*85.7 (OR) 6 CLASSIFICATIONS

1. 424*85.4 XR
08:44:25 COPY AND CLEAR PAGE, PLEASE
08:44:25 COPY AND CLEAR PAGE, PLEASE

4,885,166 424*85.7 (OR) 6 CLASSIFICATIONS

2. 424*85.7 OR
3. 435*69.51 XR
4. 435*240.27 XR
5. 435*320 XR
6. 530*351 XR

4,859,596 435*172.3 (OR) 9 CLASSIFICATIONS

1. 435*91 XR
2. 435*172.3 OR
3. 435*255 XR
4. 435*317.1 XR
5. 435*320 XR
6. 536*27 XR
7. 935*28 XR
8. 935*37 XR
9. 935*56 XR

=> log y
=> log y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 5.60 | 5.60 |

U.S. Patent & Trademark Office LOGOFF AT 08:44:41 ON 14 FEB 90

9/'U"

NO CARRIER

+++

ATZ

ATZ

OK

470

polymerase and the four dNTP's under conditions which have been described for double-stranded DNA synthesis (A. R. Davis et. . . products by electrophoresis through a 13% acrylamide gel followed by autoradiography showed that more than 80% of the starting single-stranded

08:41:55 COPY AND CLEAR PAGE, PLEASE

08:41:55 COPY AND CLEAR PAGE, PLEASE

DET0(103)

oligonucleotides were converted into double-stranded material. The DNA was isolated by passage of the reaction mix over a Sephadex G50 column. . .

US PAT NO: 4,801,536

L3: 3 of 4

DETDESC:

DET0(40)

The . . . was constructed as follows. The 4750 bp HindIII-PvuII restriction fragment from pBE3, (the first three bases of the HindIII 5' **overlap** were filled in by the **Klenow** fragment with dATP, dGTP, and dCTP), was ligated to the 470 bp SphI-NdeI restriction fragment from pALI.DELTA.5M, (the 3' **overlap** of the SphI site was chewed back by the **Klenow** fragment and the first base of the NdeI 5' overlap was filled in by the **Klenow** fragment with dTTP), to construct pFPI1. The 5200 bp BamHI-PstI restriction fragment from pFPI1, (the 3' **overlap** of PstI was removed using the **Klenow** fragment), was ligated to the 2632 bp BamHI-AhaIII restriction fragment from p4A to construct pFPIfla304. The AhaIII end of the . . . p4A was treated with "slow" Ibal-31 exonuclease before ligation, and the proper pFPIfla304 construction was screened by colony hybridization with an **oligonucleotide** (50'-T-T-A-T-T-A-C-G-T-G-G-C-A-T-G-C-A-A3') that spans the correct ligation junction. The sequences of the hybridization positives were determined to confirm the proper construction. The 1621 bp BamHI-BglI restriction fragment from pFPIfla304, (the BglI 5' **overlap** was filled in with the **Klenow** fragment and all four dNTPs), was ligated to the 3727 bp BamHI-ECoRI restriction fragment from pIEV1 (the EcoRI 5' **overlap** was filled in with the **Klenow**

08:42:18 COPY AND CLEAR PAGE, PLEASE

08:42:18 COPY AND CLEAR PAGE, PLEASE

DET0(40)

fragment and all four dNTPs) to construct the plasmid pIEV1fla304PI. The plasmid pIEV1fla304PI.DELTA.C was constructed by digesting pIEV1fla304PI with ClaI, . . .

US PAT NO: 4,657,857

L3: 4 of 4

SUMMARY:

BSUM(70)

As outlined in FIG. 5 the missing DNA fragment was obtained by the chemical synthesis of two partially **overlapping** oligomers. The Sac I site present in the **overlapping** part of the two **oligonucleotides** was introduced for two reasons: (i) to enable manipulation of the

=> s oligonucleotide?(p)klenow(p)overlap?
=> s oligonucleotide?(p)klenow(p)overlap?

588 OLIGONUCLEOTIDE?

332 KLENOW

88376 OVERLAP?

L3 4 OLIGONUCLEOTIDE?(P)KLENOW(P)OVERLAP?

=> d kwic

=> d kwic

US PAT NO:

4,885,166

not out
yet

L3: 1 of 4

DETDESC:

DETD(21)

The . . . triester method [R. L. Letsinger et al., J. Am. Chem. Soc. 98, 3655 (1976)]. Simplification of the synthesis of the **oligonucleotides** and polynucleotides is made possible by the solid phase method, in which the nucleotide chains are bound to a suitable. . . be built up enzymatically from chemically prepared short segments. For this, Khorana et al. [J. Biol. Chem. 251, 565 (1976)] use **overlapping** polynucleotide sequences from both DNA strands, which are held together in the correct arrangement by base-pairing and are then chemically. . . DNA ligase. Another possibility comprises incubating in each case one

08:40:49 COPY AND CLEAR PAGE, PLEASE

08:40:49 COPY AND CLEAR PAGE, PLEASE

DETD(21)

polynucleotide sequence from the two DNA strands with a short **overlapping** segment in the presence of the four required deoxynucleoside triphosphates with a DNA-polymerase, for example DNA-polymerase I, a **Klenow** fragment of polymerase I or T_{sub}.4 DNA polymerase, or with AMV (avian myeloblastosis virus) reverse transcriptase. The two polynucleotide sequences. . . 132 base pairs long of the human leukocyte interferon .alpha..sub.2 -gene can be built in the presence of DNA-polymerase I (**Klenow** fragment) from 4 chemically synthesised fragments 39 to 42 bases in length, a 40% saving in chemical synthesis in comparison. . .

=> d 2-4 kwic

=> d 2-4 kwic

US PAT NO: 4,859,596

L3: 2 of 4

DETDESC:

DETD(103)

As outlined in FIG. 9 the missing DNA fragment was obtained by the chemical synthesis of two partially **overlapping** oligomers. The Sac I site present in the **overlapping** part of the two **oligonucleotides** was introduced for two reasons: (i) to enable manipulation of the nucleotide sequence immediately upstream of the ATG codon including. . . J. Rossi et al., J. Biol. Chem. 257 (1982) 9226-9229) and converted into a double-stranded DNA molecule by incubation with **Klenow** DNA

13. 4,849,407, Jul. 18, 1989, Biologically active mosaic proteins; Mark J. Murray, et al., 514*12; 530*350

14. 4,816,397, Mar. 28, 1989, Multichain polypeptides or proteins and processes for their production; Michael A. Boss, et al., 435*69.6, 172.3, 243, 252.31, 252.33, 255, 320

15. 4,783,412, Nov. 8, 1988, Hybrid DNA synthesis of epidermal growth factor; Graeme I. Bell, 435*240.1, 69.4, 91, 172.1, 172.3, 252.31, 252.33, 255, 320; 536*27; 935*13, 69, 70, 71

08:37:26 COPY AND CLEAR PAGE, PLEASE

08:37:26 COPY AND CLEAR PAGE, PLEASE

16. 4,782,022, Nov. 1, 1988, Nitrogen fixation regulator genes; Alfred Puhler, et al., 435*172.3, 252.2, 252.33, 320; 536*27; 935*29, 56, 72

17. 4,775,622, Oct. 4, 1988, Expression, processing and secretion of heterologous protein by yeast; Ronald A. Hitzeman, et al., 435*69.4, 28, 37, 47, 48, 50, 69.8, 91, 172.1, 172.3, 255, 256, 320

18. 4,766,073, Aug. 23, 1988, Expression of biologically active PDGF analogs in eucaryotic cells; Mark J. Murray, et al., 435*69.4, 91, 172.3, 255, 317.1; 935*13, 28, 37

19. 4,764,593, Aug. 16, 1988, Manufacture and expression of genes for urogastrone and polypeptide analogs thereof; Allen R. Banks, et al., 530*324; 435*69.4; 530*350, 399, 820, 825, 834

20. 4,764,504, Aug. 16, 1988, Atrial natriuretic/vasodilator polypeptides; Lorin K. Johnson, et al., 514*12; 530*324, 350

21. 4,695,623, Sep. 22, 1987, Consensus human leukocyte interferon; Yitzhak Stabinsky, 530*351; 424*85.7; 435*69.51, 811; 439*15

22. 4,673,641, Jun. 16, 1987, Co-aggregate purification of proteins; Henry J. George, et al., 435*69.1, 69.3, 69.7, 69.8, 172.3, 261, 320; 530*412, 418; 935*36, 61, 73

23. 4,650,674, Mar. 17, 1987, Synergistic cytotoxic composition; Bharat B. Aggarwal, et al., 424*85.5, 85.4; 435*69.5; 514*12

=> s oligonucleotide?(p)(klenow or dna(w)polymerase)

=> s oligonucleotide?(p)(klenow or dna(w)polymerase)

08:39:05 COPY AND CLEAR PAGE, PLEASE

08:39:05 COPY AND CLEAR PAGE, PLEASE

588 OLIGONUCLEOTIDE?LEASE

332 KLENOW

4036 DNA

790 POLYMERASE

L2 124 OLIGONUCLEOTIDE?(P)(KLENOW OR DNA(W)POLYMERASE)

=> s oligonucleotide?(p)(klenow(p)overlap?

=> s oligonucleotide?(p)(klenow(p)overlap?

UNMATCHED LEFT PARENTHESIS 'P'(KLENOW'

=> s codon(w)usage
509 CODON
35802 USAGE
L1 23 CODON(W)USAGE

=> d 1-23
=> d 1-23

1. 4,898,828, Feb. 6, 1990, Ultrahigh copy number streptomycetes plasmids; Charles L. Hershberger, et al., 435*252.3, 172.3, 252.33, 252.35, 320; 536*27; 935*6, 29, 73, 75
2. 4,898,818, Feb. 6, 1990, Antitumor active substance, process for preparing the same, drug containing the substance, gene coding for the substance, vector containing the gene and recombinant microorganism; Satoru Nakai, et al., 435*69.1; 424*85.2; 435*69.5, 70.4, 172.3; 530*351
3. 4,897,471, Jan. 30, 1990, Consensus human leukocyte interferon; Yitzhak Stabinsky, 536*27; 424*85.7; 435*69.51, 320
4. 4,897,348, Jan. 30, 1990, Recombinant materials and methods for producing human connective tissue-activating peptide-III and analogs thereof; Paul H. Johnson, et al., 435*69.1, 69.2, 172.3, 252.33, 320; 536*27; 935*10, 13, 29, 41
5. 4,894,436, Jan. 16, 1990, Homologs of aprotinin produced from a recombinant host, process expression vector and recombinant host therefor and pharmaceutical use thereof; Ernst-August Auerswald, et al., 530*324
6. 4,889,919, Dec. 26, 1989, Biologically active PDGF derived A-chain homodimers; Mark J. Murray, et al., 530*351; 435*69.4, 172.3; 514*2, 8, 21; 530*350, 380, 399
08:37:10 COPY AND CLEAR PAGE, PLEASE
08:37:10 COPY AND CLEAR PAGE, PLEASE
:37:10 COPY AND CLEAR PAGE, PLEASE
7. 4,889,803, Dec. 26, 1989, Production of interferon gamma; Michel Revel, et al., 435*69.51, 172.3, 240.2, 320; 935*34
8. 4,888,282, Dec. 19, 1989, Synthetic gene for acyl carrier protein; Phillips D. Beremand, et al., 435*193, 172.1, 172.3, 235, 252.33, 320; 536*27; 935*14
9. 4,885,248, Dec. 5, 1989, Transfer vector; Paul G. Ahlquist, 435*172.3, 252.3, 252.33, 320; 536*27; 935*31, 39, 72, 73
10. 4,883,761, Nov. 28, 1989, Pertussis toxin gene: cloning and expression of protective antigen; Jerry M. Keith, et al., 435*320, 172.3, 252.33; 536*97; 935*11
11. 4,877,864, Oct. 31, 1989, Osteoinductive factors; Elizabeth A. Wang, et al., 530*324; 435*172.3, 320; 514*12; 935*13
12. 4,855,231, Aug. 8, 1989, Regulatory region for heterologous gene expression in yeast; David W. Stroman, et al., 435*69.1, 172.3, 207, 255, 256, 320; 536*27; 935*27, 36, 37, 56, 69

L1 4537 CODON
4688 USAGE
412 CODON(W)USAGE

=> s (alter or change or modif?) (5a) gene(w)expression

L2 26363 ALTER
143402 CHANGE
118345 MODIF?
117115 GENE
85064 EXPRESSION
159 (ALTER OR CHANGE OR MODIF?) (5A) GENE (W) EXPRESSION

=> s 11 and 12

L3 O L1 AND L2

=> s 11 and gene(w)expression

L4 117115 GENE
85064 EXPRESSION
159 (ALTER OR CHANGE OR MODIF?) (5A) GENE (W) EXPRESSION
O1 L1 AND GENE (W) EXPRESSION

=> s 14 and plant?

L5 229962 PLANT?
O2 L4 AND PLANT?

=> d 1-2

L6 ANSWER 1 OF 2

AN 88:199403 BIOSIS
DN 8885:100749
TI ENDOSYMBIOTIC ORIGIN AND CODON BIAS OF THE NUCLEAR GENE FOR
CHLOROPLAST GLYCERALDEHYDE-3-PHOSPHATE DEHYDROGENASE FROM MAIZE.
AU BRINKMANN H; MARTINEZ P; QUIGLEY F; MARTIN W; CERFF R
CS LAB. BIOL. MOLECULAIRE VEGETALE, CNRS UA 1179, UNIVERSITE DE GRENOBLE
I, B.P. 68, F-38402 SAINT MARTIN D'HERES CEDEX, FRANCE.
SD J MOL EVOL 26 (4). 1987. 320-328. CODEN: JMEVAU ISSN: 0022-2844
LA English

L6 ANSWER 2 OF 2

AN 88:112247 BIOSIS
DN 8885:57717
TI NUCLEOTIDE SEQUENCE OF COMPLEMENTARY DNA ENCODING THE SMALL SUBUNIT
OF RIBULOSE-1,5-BISPHOSPHATE CARBOXYLASE FROM MAIZE.
AU MATSUKA M; KANO-MURAKAMI Y; TANAKA Y; OZEKI Y; YAMAMOTO N
CS NATL. INST. AGROBIOLOGICAL RESOURCES, YATABE, IBARAKI 305.
SD J BIOCHEM (TOKYO) 102 (4). 1987. 673-676. CODEN: JOBIAQ ISSN:
0021-924X
LA English

=> d his

(FILE HOME)

L1 FILE BIOSIS
412 S CODON(W)USAGE
L2 159 S (ALTER OR CHANGE OR MODIF?) GENE (W) EXPRESSION
L3 O S L1 AND L2

470 A